

# An Information Theoretical Analysis of Human Insulin-Glucose System Towards The Internet of Bio-Nano Things

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**Abstract**—Molecular communication is an important tool to understand biological communications with many promising applications in Internet of Bio-Nano Things (IoBNT). The insulin-glucose system is of key significance among the major intra-body nanonetworks since it fulfills metabolic requirements of the body. Study of biological networks from information and communication theoretical (ICT) perspective is necessary for their introduction in the IoBNT framework. Therefore, the objective of this work is to provide and analyze for the first time in literature, a simple molecular communication model of the human insulin-glucose system from ICT perspective. The data rate, channel capacity and the group propagation delay are analyzed for a two-cell network between a pancreatic beta cell and a muscle cell that are connected through a capillary. The results point out a correlation between an increase in insulin resistance and a decrease in the data rate and channel capacity, an increase in the insulin transmission rate and an increase in the propagation delay. We also propose applications for introduction of the system in IoBNT framework. Multi-cell insulin glucose system models may be based on this simple model to help in the investigation, diagnosis and treatment of insulin resistance by means of novel IoBNT applications.

**Index Terms**—Internet of Bio-Nano Things (IoBNT), Insulin-glucose system, ICT-based modeling, Molecular communication, Insulin resistance

## I. INTRODUCTION

The vision of a cyber-physical paradigm that connects physical elements to each other for autonomous communication has allowed Internet of Things (IoT) to become a focus for major research and development efforts. With advances in nanotechnology and communication engineering, Internet of NanoThings (IoNT) was proposed to be based on synthesized materials, electronic circuits, and interaction through electromagnetic waves [1]. In contrast, Internet of Bio-Nano Things (IoBNT) was proposed with a focus on biological communications [2]. Under the IoBNT umbrella, biological cells are controlled using biochemical stimuli to perform operations such as intra-body sensing, actuation, and connectivity control.

A number of recent studies target the IoBNT field. In [3], analog filters that can be used as components for IoBNT

systems are proposed. The model for a bio-cyber interface for an advanced healthcare delivery system is proposed in [4]. A silicon nanowire BioFET as a molecular antenna for bio-cyber interfaces is proposed in [5]. IoBNT architecture revolves around the capability to communicate with biological entities and the quality of a communication network, its limitations and the supported rates can be quantified through an information and communication theory (ICT) study of the system. Thus, a key motivation for an ICT study of a biological system is its eventual integration in the wider IoBNT framework.

Molecular communication (MC) is suggested as the communication scheme between biological entities and their bio-cyber interfaces in IoBNT. Systems based on bio-nanomachines can be found all around and within us [6], [7]. Understanding this molecular signaling among living cells from ICT perspective provides novel nanonetworking directions and a deep insight into the ICT-based fundamentals of biological systems [6]. Several ICT models exist in literature for key MC systems of the human body such as the nervous system [8], [9], [10] and the gap junction communication between cardiomyocytes [11], however, to date no work targets an endocrine system from this perspective. Since the endocrine systems operate on the principles of MC, a study of the MC in these systems may give rise to an in-depth analysis of the system from a new perspective to produce novel diagnostic, management and treatment applications based on MC principles.

Endocrine system is a set of glands that produce hormones to control important functions of the body such as metabolism, growth, development, reproduction and emotions. Due to its sheer importance in metabolism, a huge body of literature focuses on the insulin-glucose endocrine system. Insulin regulates blood glucose by assisting its uptake in the body cells. It is produced in specialized pancreatic cells known as the *beta cells*. In cases when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces, a set of conditions known as *diabetes* occur. Since the insulin-glucose system effects the metabolism of other nanonetworks such as the nervous system, diabetic conditions affect them adversely as well [12]. Several mathematical models for the biochemical processes involved in the insulin-glucose system are described in literature [13], [14]. These models either take a higher level approach based on serum concentrations of insulin and glucose, describe the biochemical kinetics of the system or both of these in some cases. Since most diagnostic, management and treatment applications of the insulin-glucose system are based on MC, it is essential to

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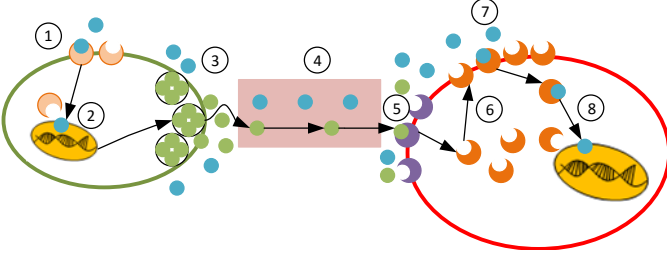


Fig. 1: Key steps of insulin-glucose system: (1) Uptake of glucose by the beta cell, (2) Glucose metabolism in the beta cell, (3) Insulin vesicle exocytosis as a result of metabolism, (4) Insulin and glucose transport by the circulatory system, (5) Insulin binding to insulin receptors at muscle cells, (6) Glucose transporter exocytosis as a result of insulin binding, (7) Glucose binding with glucose transporters and (8) Glucose transport and metabolism within the muscle cell.

model this communication such that methods to improve system performance may be discovered and IoBNT applications for this system may be realized. Therefore, in this paper, we model a simple MC system between a beta cell and muscle cell connected by means of a capillary. Expressions for data rate, bounds for channel capacity and ranges for group propagation delay are derived and the effects of insulin resistance on these communication parameters are discussed. These expressions may be used in further ICT-based models of insulin-glucose system where multi cell to multi cell connections are explored. We discuss the effect of insulin resistance on the derived ICT parameters for Type II diabetes patients. To our knowledge, this is also the first work on the ICT-based modeling of a hormonal communication channel. We also propose potential applications of IoBNT in insulin-glucose system.

The rest of this paper is organized as follows. Section II describes the insulin-glucose system that includes insulin secretion by beta cell, molecular circulation through capillaries and glucose uptake by muscle cell. ICT-based model and analysis of the system is presented in Section III. In Section IV, we present our numerical analysis based on simulations. The relationship between insulin resistance and data rate, channel capacity, propagation delay, and information transmission rate is explored in Section V. Applications of IoBNT in insulin-glucose system management are proposed in Section VI. Finally, Section VII concludes this work.

## II. INSULIN-GLUCOSE SYSTEM

In the insulin-glucose system, communication between a pancreatic beta cell and a muscle cell occurs by means of the circulatory system between them. Key steps of this process are illustrated in Fig. 1. In this section, we first present a description of the system that we model and then present processes of insulin release, transport and glucose uptake in detail.

### A. System Description

The human body is a complex system where a number of processes that are controlled by various organs work cooperatively. For instance, liver is the primary site of insulin

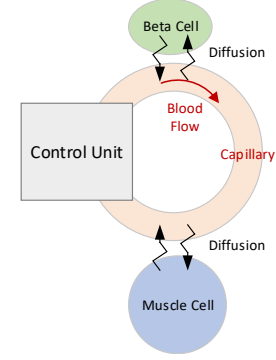


Fig. 2: System description for a cell-to-cell communication system between a beta and a muscle cell.

clearance in the human body, where approximately 80% of endogenous insulin is removed while the remainder is cleared by the kidneys and muscles, and the human heart provides the pumping force to deliver the blood to various parts of the body [15]. The modeling of all these organs along with all the different types of body cells is beyond the scope of any single study and therefore, in the current study, a hypothetical control system is assumed to perform functions similar to those performed by a number of organs in the human body such as the heart, liver, stomach, kidneys and muscle cells other than the target receiving cell. The purpose of assuming a control unit that oversees all these operation is to isolate a single beta and muscle cell only such that their mutual communication can be focused in detail.

In our model, we consider that a unit volume of the same blood is being circulated by an external control source through a capillary with an average velocity,  $v_{avg}$  as shown in Fig. 2. The capillary runs from a region that includes a beta cell in the extracellular space towards a region with a muscle cell in the extracellular space. We assume that the conditions on the boundaries of the capillary are such that the blood leaving the muscle cell end enters from the beta cell end to complete the circulation path.

Apart from pumping, the control source is responsible for controlling the insulin concentration  $I(t)$  between a minimum  $I_0$  and a maximum level  $I_{max}$ . Similarly, glucose concentration  $G(t)$  is maintained between  $G_0$  and  $G_{max}$ . These considerations ensure that the system does not suffer a runaway condition where either insulin or glucose increases in an unbounded manner. In a real life scenario, the minimum concentration of glucose and insulin can be calculated by a fasting glucose test whereas the maximum concentration can be calculated by a glucose tolerance test. Additionally, the control source is also responsible for fixed removal of insulin and glucose with rates  $l_1$  and  $l_4$ , respectively, for the introduction an external glucose impulses,  $\delta(t)$ , into the system if required, and to maintain the temperature of the system on a physiological value of  $37^\circ C$ . The assumptions provided above are similar to those in the human body under normal physiological conditions and mimic the effects of various organs such as the heart, liver and the stomach.

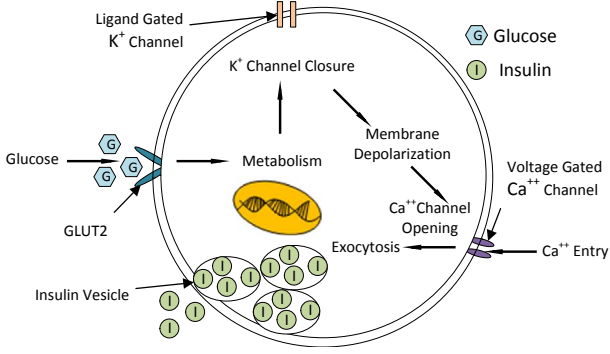


Fig. 3: Insulin secretion as a result of glucose uptake by a beta cell.

### B. Insulin Secretion

The complete process of insulin secretion from a beta cell is detailed in Fig. 3. The introduction of meal impulse,  $\delta(t)$ , increases  $G(t)$  and thus, the probability of glucose molecule reception by the beta cells,  $P(B_G)$ , through their GLUT2 glucose sensors [16]. Once received, the glucose is transported inside the cell to be metabolized. This causes the concentration of Adenosine triphosphate (ATP) to increase, which, in turn, causes the ligand-gated  $K^+$  channels to shut down. Thus, the membrane potential starts to increase since  $K^+$  ions are not flowing out anymore. Increase of membrane potential causes the voltage-gated  $Ca^{++}$  channels to open and an inflow of  $Ca^{++}$  ions occurs. The increased membrane potential causes insulin vesicles to move towards the cell membrane, where insulin is released by exocytosis [17]. All the processes described above are governed by chemical kinetics and the values of most kinetic constants are already known in literature [14].

The insulin concentration is based on the average clearance rate of insulin, its nominal release rate without glucose and the net increase of insulin release rate due to the presence of glucose [18]. The change of insulin concentration, i.e.  $I(t)$  with respect to time can be described by

$$\frac{dI(t)}{dt} = -l_1 I(t) + n_I + l_3 G(t), \quad (1)$$

where  $l_1 I(t)$  represents the average rate of insulin clearance independent of glucose,  $n_I$  is the average rate of basal insulin release by the beta cell independent of glucose and  $l_3 G(t)$  is the net increase in the rate of insulin release as a result of increase in glucose concentration  $G(t)$ . Since the insulin leakage governed by  $n_I$  is independent of any glucose impulse, it represents a source of noise in the secretion process.

The probability of glucose molecule reception by the beta cells,  $P(B_G)$ , is directly proportional to the glucose concentration  $G(t)$  and the number of GLUT2 transporters present on the surface of the beta cell.  $P(B_G)$  can be expressed as

$$P(B_G) = \frac{G(t) - G_0}{G_{max} - G_0} \times \frac{N_{act2}}{N_{GLUT2}}, \quad (2)$$

where  $N_{act2}$  is the number of unbound GLUT2 transporters on the surface of a beta cell and  $N_{GLUT2}$  represents the total number of GLUT2 receptors in a beta cell. After a glucose

impulse,  $G(t)$  increases above  $G_0$  causing an increase in  $P(B_G)$ . The same happens if the number of GLUT2 receptors on the surface of a beta cell increase to fulfill the metabolic requirements of the beta cell.  $I(t)$  also depends on  $P(B_G)$  since the release of insulin depends on the glucose sensing by the GLUT2 transporters.

### C. Circulation

Blood circulation provides the mechanism for insulin and glucose delivery to the beta and the muscle cells. In a normal human body, this transport occurs through various arteries and veins of the body that are then connected by networks of capillaries. Capillaries are the smallest type of blood vessels ranging from 5 to  $40\mu m$  in diameter with characteristic high surface area to volume ratios that maximizes the potential for blood-tissue exchange [19].

Considering the case of two specific cells connected through a capillary, there are three important components of the transport for insulin molecules as shown in Fig 2. These are

- diffusion of the molecules from the beta cell towards the capillary,
- transport through the capillary, and
- diffusion from the capillary to the muscle cell.

For diffusion towards and from the capillary, we consider that the forces of flow inside the capillary do not effect the insulin molecules. Thus, this movement of molecules in the extracellular space can be modeled by Brownian motion that results from thermal motion of molecules within the fluid. We ignore collisions between the messenger molecules, as reported extensively in the literature for MC [8], [10], [20], [21], therefore the molecule experiences Gaussian displacement. The diffusion equation describes diffusion as

$$\frac{\partial I(x, t)}{\partial t} = D \nabla^2 I(x, t), \quad (3)$$

where  $I(x, t)$  denotes the insulin concentration and  $D$  denotes the diffusion coefficient which depend on temperature, pressure and the viscosity of the blood. Equation (3) is linear time-invariant and the solution in an  $n$ -dimensional space from a position  $x$  is calculated by the Green's function as

$$Gr(x, t) = (4\pi Dt)^{-n/2} e^{-\frac{(x-x')^2}{4Dt}}. \quad (4)$$

Note that (4) indicates how a point of probability density initially at point  $x$  diffuses over  $n$ -dimensional space and time existing under the condition of normalization given as

$$\int_{-\infty}^{\infty} Gr(x, t) dx = 1, \quad (5)$$

where the normalization is achieved by the multiplication of a normalization constant that is calculated numerically. Inside the capillary, insulin molecules are transported by the blood flow. This causes a convective flow process where along with the flow forces, diffusion of the particles also occurs. Reynold's number is used to help predict flow patterns in different fluid flow situations with low Reynold's numbers characterizing laminar flows and high Reynold's numbers

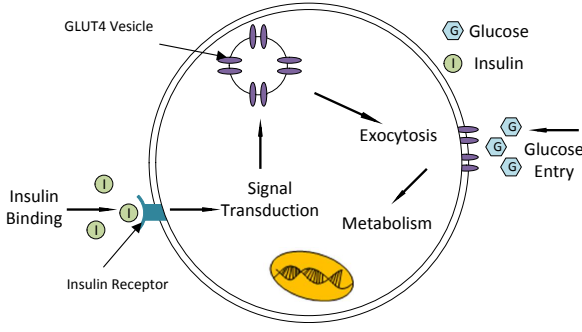


Fig. 4: Glucose uptake by a muscle cell as a result of insulin binding.

representing turbulent flow. The Reynold's number,  $Re$ , is given as

$$Re = \frac{\rho v_{avg} d_H}{\nu}, \quad (6)$$

where  $\rho$  is the fluid density,  $v_{avg}$  is the mean fluid velocity,  $d_H$  is the hydraulic diameter and  $\nu$  represents the fluid viscosity. The Reynold's number for capillaries is very low, i.e. 0.001 meaning that there is laminar flow within capillaries that causes flow in parallel layers with no mixing between the layers [19]. This leads to the conclusion that Brownian motion within the capillary can be neglected on a microscale in comparison to the laminar flow forces [22].

Therefore, the average propagation time for insulin molecules from a beta cell through a capillary with length  $L$  to a muscle cell is given as

$$T_C = \frac{L}{v_{avg}} + \int_0^\infty t Gr_b(x, t) dt + \int_0^\infty t Gr_m(x, t) dt. \quad (7)$$

Here,  $Gr_b(x, t)$  represents the normalized Green's function diffusion from the beta cell to the capillary and  $Gr_m(x, t)$  represents the normalized Green's function diffusion from the capillary to the muscle cell.

#### D. Glucose Uptake

GLUT1 and GLUT3 glucose transporters are available throughout the cells of muscles and tissues to maintain a basal uptake of glucose [23]. However, since for the current study we look at the insulin mediated glucose uptake, they are neglected in Fig. 4, which shows the process of glucose uptake by a muscle cell. The muscle cell begins glucose uptake when insulin molecules bind to insulin receptors present on the cell membrane. Insulin receptors are protein molecules that can bind to smaller insulin ligands that act as agonists, making the receptor to function. Until this happens, 'GLUT4', the major insulin dependent glucose transporters, remain in vesicles inside the cell. As soon as the insulin binds, signals are sent to the GLUT4 vesicles and exocytosis of the vesicles starts [17]. This, in turn, allows GLUT4 to transport glucose inside the cell that is then used for metabolism. Outside the cell, overall glucose concentration decreases as a result of the uptake. This then reduces the production of insulin from beta cell as well [18].

The change in glucose concentration is a sum of average blood glucose removal rate, release of glucose by the control unit independent of  $\delta(t)$ , its insulin mediated glucose uptake and  $\delta(t)$  that leaves the system with a big concentration of glucose [18]. This can be expressed as

$$\frac{dG(t)}{dt} = -l_4 G(t) + n_G - l_6 I(t) + \delta(t), \quad (8)$$

where  $l_4 G(t)$  represents the average rate of glucose removal independent of insulin,  $n_G$  is the average rate of basal glucose release and  $l_6 I(t)$  is the net increase in the rate of glucose uptake due to the presence of insulin. Similar to the secretion process,  $n_G$  represents a noise source in the glucose uptake process that can be

The probability of insulin reception at the muscle cell,  $P(M_I)$ , is directly proportional to the insulin concentration  $I(t)$  as well as the number of insulin receptors present on the cell. Therefore,  $P(M_I)$  can be written as

$$P(M_I) = \frac{I(t) - I_0}{I_{max} - I_0} \times \frac{N_{ub}}{N_t}. \quad (9)$$

Here,  $N_{ub}$  is the number of unbound insulin receptors and  $N_t$  represents the total number of insulin receptors on the cell membrane of a muscle cell.

In case of a fasting test, a person is not allowed to have any food for 8 to 12 hours before the test [18]. This lack of a digestive impulse  $\delta(t)$  forces  $I(t)$  and  $G(t)$  to their minimum values  $I_0$  and  $G_0$ , respectively. Additionally,  $\frac{dI(t)}{dt} = 0$  and  $\frac{dG(t)}{dt} = 0$ , since there are no changes in the insulin or glucose concentrations. For such a scenario, (1) and (8) can be written as

$$n_I = l_1 I_0 - l_3 G_0, \quad (10)$$

$$n_G = l_4 G_0 + l_6 I_0. \quad (11)$$

Equations (1), (8), (10) and (11) can be used to give a solution for glucose concentration  $G(t)$  similar to [18]

$$G(t) = G_0 + A e^{-\alpha t} \sin(\omega t) \quad (12)$$

where  $A$  is the undamped amplitude,  $\alpha = \frac{1}{2}(l_1 + l_4)$  represents the independent clearance rates of glucose and insulin, and  $\omega^2 = \omega_0^2 - \alpha^2$  with the natural response  $\omega_0^2 = l_1 l_4 + l_3 l_6$  representing the control unit's response.

### III. INFORMATION THEORETIC MODEL OF INSULIN-GLUCOSE SYSTEM

For the information theoretical model of the insulin-glucose system, we consider insulin and glucose as information molecules. Although these molecules occupy the same physical channel (capillary), they operate in two different channels as illustrated in Fig. 5.

As an abstraction of MC in the forward channel, we consider the release of insulin molecules by the beta cell as a transmission process. This transmission occurs based on the feedback of glucose concentration by the GLUT2 transporters. Each insulin molecule is considered as an independent transmission bit that may be received by the muscle cell separately to constitute the reception process. It should be noted here that since all insulin molecules are similar, the information they

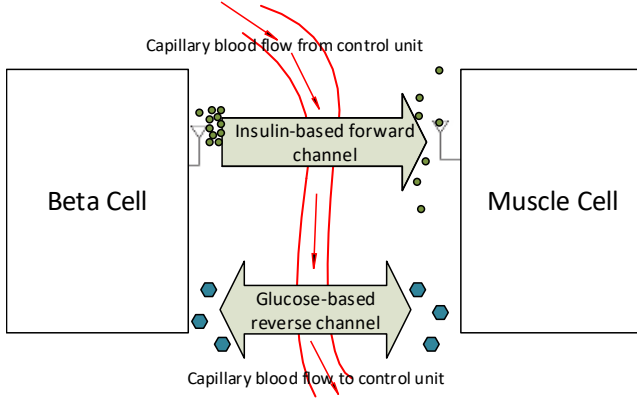


Fig. 5: ICT model of insulin-glucose system.

carry is also similar. After the reception process, the muscle cell uptakes glucose from the blood stream by exocytosis of GLUT4.

In the feedback channel, depending on the uptake of glucose by the muscle cell, glucose concentration changes. Thus, glucose molecules constitute the information carriers of the feedback channel. The purpose of this feedback channel is to communicate the channel state information (CSI) with both the transmission (by beta cell) and the reception processes (by muscle cell). The management of the feedback channel is the primary responsibility of the control unit as evident from (12).

#### A. Channel Capacity

In the current scenario, we define channel capacity as the maximum number of insulin molecules that can be communicated per unit time. On a molecular observation scale, each insulin receptor on the muscle cell works independently, and each molecule that is communicated constitutes a different data reception event. Considering  $N_t$  as the total number of transmitted insulin molecules at a particular instant in the unit volume supported by the control unit,  $I(t)$  is related to  $N_t$  as [24]

$$N_t = 7.174 \times 10^{-12} \times A_v \times I(t), \quad (13)$$

where  $A_v$  is a Avogadro's number. Even for a unit concentration of insulin per mL, the above number is quite large in comparison to the total number of receptors ( $N_r$ ) available on the muscle cell.

The instantaneous data rate of the insulin-glucose system is equal to the number of insulin-insulin receptors bindings at any time. Thus, the change of data rate with respect to time is equal to receptor binding rate of insulin at the receiver muscle cell that is governed by the kinetic equation

$$\frac{\partial R(t)}{\partial t} = k_f I(t) N_{ub} - k_r R(t), \quad (14)$$

where  $R(t)$  is the instantaneous data rate of the insulin-glucose system that represents the number of insulin-receptor bound pairs,  $k_f$  is the forward binding rate of insulin and  $k_r$  is the reverse binding rate with the values of  $k_f$ , and  $k_r$  already provided in literature [14]. Insulin concentration and receptor density at the receiver both are important factors that contribute towards a higher data rate.

At equilibrium, the data rate change becomes zero ( $\frac{\partial R(t)}{\partial t} = 0$ ) and the equilibrium data rate is given as

$$R_{eq} = \frac{N_{eq} I_{eq}}{k_D}, \quad (15)$$

where  $N_{eq}$  is the number of unbound receptors at equilibrium,  $I_{eq}$  is the equilibrium concentration of insulin and  $k_D = k_r/k_f$  is disassociation equilibrium constant. For the small values that  $k_D$  typically has, the capacity of the muscle cell turn out to be high. If we compare two scenarios for the reception, one with a higher  $k_D$  and the other with a lower  $k_D$ , the data rate will be higher in the second case, and thus it will be able to detect smaller changes in the concentration of insulin in comparison to the first system. The equilibrium is an important point for the calculation of data rate since the number of insulin-insulin receptor pairings equals the number of separations.

The total number of receptors,  $N_r$ , is a sum of bound receptors,  $R_{eq}$  and the unbound receptors,  $N_{eq}$ . Therefore, (15) can be modified as

$$R_{eq} = \frac{(N_r - R_{eq}) I_{eq}}{k_D}, \quad (16)$$

which can be solved for equilibrium capacity as

$$R_{eq} = \frac{N_r I_{eq}}{k_D + I_{eq}}. \quad (17)$$

Since channel capacity is the maximal bound of data rate, we consider the case when negligible noise and attenuation is faced by transmitted insulin molecules in the channel. This results in the receivers acting as parallel channels and the channel capacity equals the least number of transmissions or receptions, or the maximum number of insulin molecules that can be contained in a capillary provided the receptors and insulin molecules are infinite, i.e.,

$$C = \min(N_t, N_r, N_{max}), \quad (18)$$

where  $N_{max}$  represents the maximum number of insulin molecules that can be contained in the capillary. The diameter of capillaries is several orders of magnitude higher than that of an insulin molecule, therefore, usually  $\min(N_t, N_r)$ . As stated earlier, the number of insulin receptors is normally much less than the number of insulin molecules to facilitate the easy binding of insulin. Therefore, under normal cellular operation  $C = N_r$ . This, however, may not be the case every time because insulin pools present in a beta cell can be spent as a result of disease or persistent glucose impulses. In such cases,  $C = N_t$ .

#### B. Channel Propagation Delay

The average channel propagation delay for a group of insulin molecules to traverse from the beta cell to receivers on the muscle cell in a first-hit scenario is a sum of the time taken for vesicle release  $T_{ves}$ , time taken for capillary propagation  $T_C$  and the time required for binding with the insulin receptors at the muscle cell  $T_{bind}$ . This delay increases in case either of  $P(B_G)$  or  $P(M_I)$  reduce [14], [25]. Therefore, total average group delay  $T$  is given as

$$T = \frac{1}{P(B_G) \times P(M_I)} (T_{ves} + T_C + T_{bind}). \quad (19)$$



TABLE I: Values of key physiological variables [26], [27], [28].

Parameter	Physiological Value
$v_{avg}$	1.14mm/sec
$k_D$	3nm
$T_{ves}$	100msec
$T_{bind}$	100msec
Body temperature	37°C

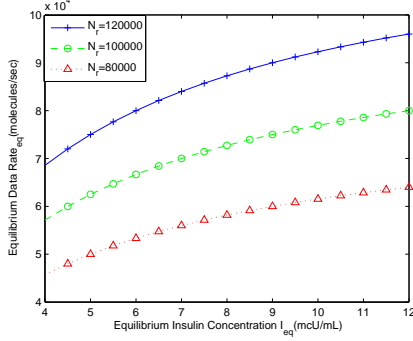


Fig. 6: Effect of insulin concentration on equilibrium data rate for different number of insulin receptors.

The probability product,  $P(B_G) \times P(M_I)$ , plays the most important part in increasing the propagation delay. As we will see in the Section V, physiological diseases cause either one or both of these parameters to decrease, increasing the overall propagation delay.

The  $T_C$  in (19) can be the delay for a single capillary or the transport through various arteries and capillaries. In [29], the authors present a detailed model of transport through larger regions of circulatory system that may be employed in case larger networks are considered. It should be noted that vesicle release and insulin binding are usually on the order of a few hundred milliseconds, whereas the transport delay through a capillary and the diffusion from the capillary usually takes up several seconds [28], [26]. Therefore, for a capillary with a sufficiently long length or for a large network of blood vessels,  $T_{ves}$  and  $T_{bind}$  may be neglected.

#### IV. NUMERICAL ANALYSIS

In this section, we present numerical analysis of the insulin-glucose model for the data rate, insulin transmission rate and the group propagation delay to show how these parameters change with the properties of the system.

For the numerical analysis, we consider a single beta cell connected to a muscle cell through a capillary channel as shown in Fig. 1. The distance between the capillary and either of the cells is considered as unit to simplify the diffusion analysis. Important values for various physiological variables used for the current analysis are presented in Table I.

##### A. Data Rate

Using (17), we can evaluate equilibrium data rate,  $R_{eq}$ , for various insulin concentrations.  $I_{eq}$  values between 4 – 12  $\mu U/mL$  are selected from human physiology and results

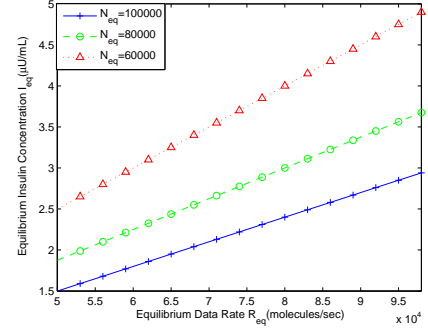


Fig. 7: Effect of data rate on insulin concentration for different number of equilibrium receptors.

are generated for different number of insulin receptors ( $N_r$ ). The various values of  $N_r$  used for the simulation are provided for mammalian cell physiology in [30].

The result of the simulation is shown in Fig. 6. We can observe that  $R_{eq}$  increases with an increase in the insulin concentration. However, this increase slows down at higher concentrations. The result also shows that  $R_{eq}$  is proportional to the total number of insulin receptors present on the cell surface. However, we also note that only a small percentage of the total receptors are used in the reception process and the maximum limit of capacity from (17) for each of the cases may be achieved only at very high concentrations of insulin. Since  $I_{max}$  is regulated by the control unit, the system cannot go beyond that point to a higher value. Additionally, high concentrations are beyond the levels of normal insulin concentration in the normal human body. This means that under normal conditions, the insulin-glucose operates much below its theoretical maximal capacity limits, thus, ensuring a reliable information transfer across the system. This behavior is seen in many biological MC systems, which operate much below the maximal capacity bounds to ensure reliable information transfer [6].

##### B. Insulin Transmission Rate

In order to observe the impact of data rate on the insulin concentration, which acts as a measure of insulin transmission rate, Fig. 7 is generated using (15). Firstly, the result shows that  $N_{eq}$  is inversely proportional to the  $I_{eq}$  required to achieve a certain data rate. Secondly, we observe that as data rate increases, the insulin concentration required to achieve it increases in an unbounded manner. Though not shown by the current figure, this unbounded increase cannot go beyond  $I_{max}$  set by the control system and in such a case the system goes into a saturation. An unbounded increase is practically not possible in the human body for the pancreatic beta cell because the insulin pools in a beta cell can provide insulin up to a certain level before depleting the reserves and any regeneration may need further time. Physically such conditions drive the beta cell in an overdrive mode to produce more insulin and reduce the overall cell life.

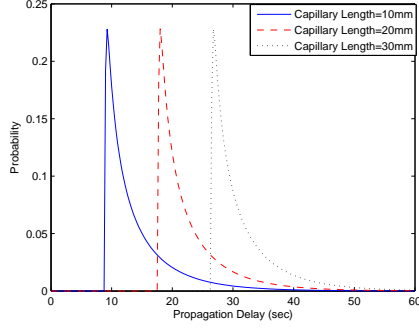


Fig. 8: PDF of average propagation delay through capillaries of various lengths.

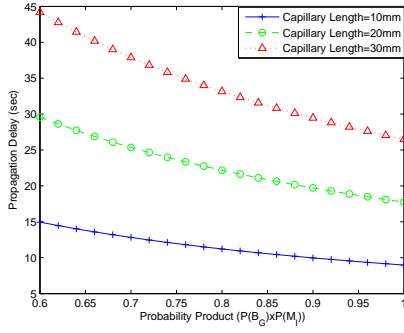


Fig. 9: Effect of probability product on average propagation delay.

### C. Channel Propagation Delay

Considering 1-dimensional diffusion, the probability density functions (PDF) of  $T_C$ , the average propagation delay for a group pf insulin molecules through capillaries of various lengths, is shown in Fig. 8 using (4), (5) and (7) in a first-hit scenario.  $T_C$  is proportional to capillary lengths, however, it can be observed that delays due to diffusion are also quite significant. This means that diffusive delays cannot be neglected for analysis of capillary based transport systems for short lengths of capillaries.

The effects of probability product  $P(B_G) \times P(M_I)$  on the total propagation delay is shown in Fig. 9. The result shows that as the probability product increases, the delay decreases. In the absence of a glucose impulse,  $P(B_G)$  reduces, and thus the product term increases the overall average propagation delay. Similarly, if insulin concentration is reduced,  $P(M_I)$  increases the average propagation delay.

## V. INSULIN RESISTANCE AND ICT-BASED METRICS FOR THE INSULIN-GLUCOSE SYSTEM

As of 2014, among the population that suffers from diabetes, 90% cases suffer from Type 2 Diabetes that is characterized by insulin resistance [31]. Insulin resistance is a physiological condition, where the body cells fail to respond to insulin and reduce the uptake of glucose leading to a high blood sugar level [32]. Beta cells subsequently increase their production of insulin, further contributing to a high blood insulin level.

TABLE II: Effect of diabetes on trends of different communication parameters as a result of insulin resistance and reduced insulin production.

Parameter	Insulin Resistance	Reduced Insulin Production
Number of receivers		no effect
Number of transmitters	no effect	↓
Data rate	↓	↓
Channel capacity	↓	↓
Transmission rate	↓	↓
Propagation delay	↑	↑

Since the body cells cannot uptake glucose for metabolism, the energy production of the body decreases [32]. As the disease progresses, the insulin production itself decreases as a result of diminished insulin pools in the beta cells and premature death of beta cells. The effects of these conditions on the trends of data rate, channel capacity, transmission rate and propagation delay are summarized in Table II. We discuss the details of these scenarios further in the following.

### A. Effects on Data Rate and Channel Capacity

A significant number of insulin receptors do not activate in response to insulin binding as a result of insulin resistance [33]. This causes a failure in the reception process and slows down the glucose uptake. From the perspective of the model presented, this means a reduction  $N_r$  present on the muscle cells. Equation (13) shows us that  $N_t$  is quite high in comparison to  $N_r$ . Additionally, from (17) and (18), we see that a reduction in  $N_r$  affects the data rate since the bound of channel capacity for the insulin-glucose system is the maximum number of receptor present on the muscle cells. Therefore, both the data rate and the channel capacity of the insulin-glucose system decrease as a result of insulin resistance. This inference is also possible from Fig. 6, where we see that the number of insulin receptors is directly proportional to data rate. The case for reduced insulin production is also similar, where a reduction in the insulin concentration decreases the overall channel capacity.

### B. Effects on Insulin Transmission Rate

Since the effective number of insulin receptors decreases as a result of insulin resistance, we observe from (15) and Fig. 7 that the production of insulin also increases. This results in high blood insulin, which is a major symptom of Type 2 diabetes [34]. Additionally, since the beta cell is forced to produce higher amounts of insulin, it needs to work more and this eventually causes the cell life to reduce. This often happens in late diabetes cases, where starting from insulin resistance, the beta cells are lost as well, thus, compounding the problems of a diabetic patient [31].

### C. Effects on Channel Propagation Delay

The concentration of both glucose and insulin increases as a result of insulin resistance. At first glance, this may seem like an increase in both  $P(B_G)$  and  $P(M_I)$  and such a scenario should reduce the average channel propagation delay,

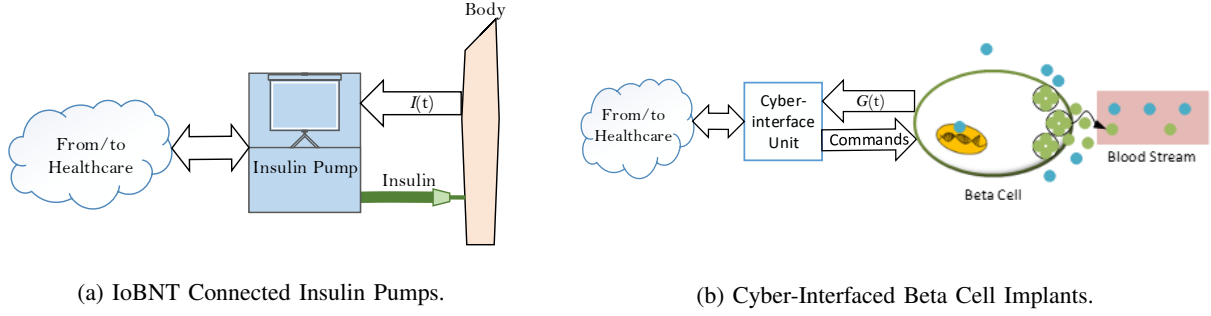


Fig. 10: Applications of insulin-glucose system towards IoBNT.

however, this is not the case. Studies have found the reduction of insulin receptors during insulin resistance by goes up to 75 – 80% of their total numbers [35]. This reduces  $P(M_I)$  by (9) and causes a reduction in the corresponding number of active GLUT4 transporters at the muscle cell membrane. Thus, the overall effect is an increase in the average channel propagation delay of the insulin-glucose system.

## VI. INSULIN-GLUCOSE SYSTEM TOWARDS IOBNT

Insulin-glucose system can be the target of a number of important IoBNT applications. In the following we discuss some possible application that aim towards the introduction of insulin-glucose system described in the current work towards the IoBNT framework.

### A. IoBNT Connected Insulin Pumps

Efficient insulin supply by means of subcutaneous insulin pumps can be an important step towards diabetes management. Subcutaneous insulin pumps are already realized [36], [37], however, the current generation of insulin pumps is *offline*, where standalone insulin pumps with a small supply of insulin, release it at preprogrammed times or according to the local glucose concentration of the body area surrounding the pump. We envision that these device can be operated *online* as a part of the IoBNT framework as shown in Fig. 10 (a). Important parameters for diabetes management such as insulin and glucose concentrations can be directly communicated to health care providers in such systems. Apart from the obvious benefit of providing detailed disease progression being online, the proposed systems can improve pump efficiencies by several orders making the insulin cartridge last longer. Such systems can also protect the body from the effects of excessive blood insulin [38].

### B. Cyber-Interfaced Beta Cell Implants

Implantation of pancreatic islets is suggested by some experiments to manage insulin-dependent diabetic patients [39]. As an application of IoBNT, we propose that insulin pumps may be replaced altogether by cyber-interfaced beta cells that can be implanted as systems for the manufacture of insulin upon triggers from IoBNT remote health monitoring setups as shown in Fig. 10 (b). The analysis we presented in this paper can also be considered for such a scenario where a cyber-connected beta cell is interface with a muscle cell.

### C. Energy Harvesting for IoBNT Applications

Since the insulin-glucose system is metabolically connected with other networks of the body, it may also be considered as an energy resource for intra-body IoBNT implants. In such cases, bio-cyber interfaces, sensors, actuators and even synthesis of drugs may be powered by the energy supplied by the insulin-glucose system. These systems require the biological implants to be engineered with glucose receptors and insulin receptors. Our analysis in this work remains aligned with goal if such a IoBNT implant is considered instead of a muscle cell.

## VII. CONCLUSION

In this paper, we provide and analyze a molecular communication model of the insulin-glucose system from the ICT perspective. Insulin and glucose molecules are considered as modulated molecular information carriers. These two molecules operate simultaneously in the system in a single physical channel, making a forward and a feedback channel operating on insulin and glucose molecules, respectively. The data rate, channel capacity, propagation delay for a group of insulin molecules and the insulin transmission rate are analyzed for a two-cell network between one pancreatic beta cell and a receiving muscle cell, connected through a capillary. Reduction in the number of receptor elements due to insulin resistance is also investigated. The results of analyses point out a correlation between an increase in insulin resistance and a decrease in the data rate and channel capacity, an increase in the transmission rate and an increase in the propagation delay. The model and results of this work may help in the investigation, diagnosis and treatment of insulin resistance by means of novel ICT-based technologies. Further research on the connections between major nanonetworks of the body such as the nervous system and the insulin-glucose system may benefit from this work. The model may pave way for future applications of IoBNT such as the management of insulin resistance by increasing the efficiency of insulin pumps.

## ACKNOWLEDGMENT

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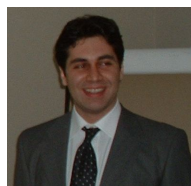


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